

Serial No.: 10/691,330

Confirmation No.: 1384

Filed: October 22, 2003

For: USE OF COLOSTRININ, CONSTITUENT PEPTIDES THEREOF, AND ANALOGS THEREOF AS
INHIBITORS OF APOPTOSIS AND OTHER CELLULAR DAMAGE

Remarks

The Office Action mailed October 25, 2006 has been received and reviewed. Claims 25-32 having been added, claims 1-6, 8, 12-15, and 25-32 are pending. Reconsideration and withdrawal of the rejections are respectfully requested.

Traversal of Restriction Requirement

Applicants continue to traverse the Restriction Requirement mailed February 8, 2005. As discussed in more detail below, Applicants respectfully submit that the rejection of claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,500,798 is improper. However, if the Examiner continues to maintain this obviousness-type double patenting rejection, Applicants submit that all thirty-four sequences of SEQ ID NO:1-34 must properly be examined in the present application. Claims 1-8 of U.S. Patent No. 6,500,798 are drawn to SEQ ID NO:1 through SEQ ID NO:34. Thus, SEQ ID NO:1 through SEQ ID NO:34 have been previously searched and examined by the U.S. Patent and Trademark Office. If the Examiner continues to maintain that the methods of the present invention and the methods of U.S. Patent No. 6,500,798 are not patentably distinct, and as each of SEQ ID NO:1-34 have already been searched and examined by the U.S. Patent and Trademark Office, Applicants submit that methods drawn to SEQ ID NO:1 through SEQ ID NO:34 can be readily examined in the present application without placing undue burden on the Examiner. Thus, Applicants submit that new claims 25 and 26 properly belong with the present invention.

Applicants further submit that, if the Examiner's rejection of claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,903,068 is maintained, new claims 29 and 30 properly belong with the present invention.

Further, Applicants submit that, if the Examiner's rejection of claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being

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unpatentable over claims 1-7 of U.S. Patent No. 7,119,064 is maintained, new claims 31 and 32 properly belong with the present invention.

Finally, Applicants submit that, if the Examiner's obviousness-type double patenting rejections of pending claims 1-6, 8, and 12-15 over U.S. Patent No. 6,500,798, U.S. Patent No. 6,903,068, and U.S. Patent No. 7,119,064 is maintained, new claim 27 (drawn to a "method for reducing the toxic effect of β -amyloid on a cell . . . comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, and combinations thereof"/Group II in the Restriction Requirement mailed February 8, 2005) and new claim 28 (drawn to a "method for reducing the toxic effect of retinoic acid on a cell . . . comprising contacting the cell with an effective amount of a compound selected from the group of colostrinin, a constituent peptide thereof, and combinations thereof"/Group III in the Restriction Requirement mailed February 8, 2005) properly belong with the present invention.

The examination of new claims 25-32 along with the invention of claims 1-6, 8, and 12-15 is respectfully requested.

Double Patenting Rejection over claims 1-8 of U.S. Patent No. 6,903,068

Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,903,068 (the '068 patent). This rejection is respectfully traversed.

Applicants submit that claims 1-6, 8, and 12-15 of the instant application and claims 1-10 of the '068 patent are drawn to methods that are patentably distinct from each other because the methods steps and outcomes are completely different.

Specifically, the pending claims of the instant application are drawn to methods "for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor . . . wherein the apoptosis inhibitor inhibits apoptosis in the cell" (claim 1-6 and 8) and "for protecting against DNA damage in a cell, the method comprising

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contacting the cell with an effective amount of a compound . . . wherein the compound protects the cell against DNA damage" (claims 12-15).

In contrast, claims 1-10 of the '68 patent are drawn to methods "for inducing a cytokine in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine" (claims 1-5) and "for modulating an immune response in a cell, the method comprising contacting the cell with an immunological regulator under conditions effective to induce a cytokine" (claims 6-10).

Applicants respectfully submit that the Examiner has failed to provide the necessary nexus to substantiate the assertion that the methods of instant claims 1-6, 8, and 12-15 are "obvious variations" of claims 1-10 of the '068 patent. The Examiner repeatedly relies on teachings that "colostrinin induces a variety of cytokines in leukocytes or modulates cytokine production" (see pages 4-5, Office Action mailed October 25, 2006, and page 2, Advisory Action mailed January 18, 2007) to substantiate a conclusion that claims 1-6 and 8 of the instant application (drawn to methods for inhibiting apoptosis and for protecting against DNA damage in a cell) are obvious variants of claims 1-10 of the '068 patent (drawn to inducing a cytokine in a cell). Applicants respectfully submit that no teachings in the '068 patent, the instant application, nor in any references provided by the Examiner substantiate the assertion that methods for inducing a cytokine in a cell (the '068 patent) make obvious methods for inhibiting apoptosis and for protecting against DNA damage in a cell (the instant application).

Further, Applicants respectfully submit that the '068 patent does not support a rejection of the present claims under 35 U.S.C. §102(e) or 35 U.S.C. §103 (see, for example, the Examiner's withdrawal of the rejection of claims 1-15 as anticipated by the '068 patent (page 2, Office Action mailed June 8, 2006)). Thus, Applicants' submit that claims 1-6, 8, and 12-15 cannot be rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of the '068 patent.

In view of the above discussion, reconsideration and withdrawal of the rejection of pending claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double

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patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,903,068 is respectfully requested.

Double Patenting Rejection over claims 1-7 of U.S. Patent No. 7,119,064

Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7,119,064 (the '064 patent). This rejection is respectfully traversed.

Applicants submit that claims 1-6, 8, and 12-15 of the instant application and claims 1-7 of the '064 patent are drawn to methods that are patentably distinct from each other because the methods steps and outcomes of claims 1-6, 8, and 12-15 of the instant application when compared to claims 1-7 of the '064 patent are wholly different.

Specifically, the pending claims of the instant application are drawn to methods "for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor . . . wherein the apoptosis inhibitor inhibits apoptosis in the cell" (claim 1-6 and 8) and "for protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of a compound . . . wherein the compound protects the cell against DNA damage" (claims 12-15).

In contrast, claims 1-7 of the '064 patent are drawn to methods "of modulating an intracellular signaling molecule in a cell, the method comprising contacting the cell with an effective amount of a modulator . . . under conditions effective to accomplish at least one of the following: reduce 4-hydroxynonenal (4HNE)-protein adduct formation; inhibit 4HNE-mediated glutathione depletion; inhibit 4HNE-induced activation of p53 protein; or inhibit 4HNE-induced activation of c-Jun NH₂-terminal kinases" (claims 1-6) and "of down regulating the 4-hydroxynonenal (4HNE)-mediated oxidative damage associated with lipid peroxidation in a cell, the method comprising contacting the cell with an effective amount of a modulator . . . wherein 4HNE-mediated oxidative damage associated with lipid peroxidation in the cell is down regulated" (claim 7).

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In rejecting pending claims 1-6, 8, and 12-15, the Examiner asserted that "the specification indicates 4-HNE (4-hydroxynonenal) induces apoptosis (Example 7, page 28)" (page 7, Office Action mailed October 25, 2006) and thus, the presently claimed method for inhibiting apoptosis and for protecting against DNA damage are "obvious variations" of the methods of claims 1-7 of U.S. Patent No. 7,119,064. Applicants disagree and submit that knowledge that 4-HNE induces apoptosis in no manner substantiates the Examiner's assertion that the presently claimed methods for inhibiting apoptosis and for protecting against DNA damage in a cell are obvious variants of methods "of modulating an intracellular signaling molecule in a cell, the method comprising contacting the cell with an effective amount of a modulator . . . under conditions effective to accomplish at least one of the following: reduce 4-hydroxynonenal (4HNE)-protein adduct formation; inhibit 4HNE-mediated glutathione depletion; inhibit 4HNE-induced activation of p53 protein; or inhibit 4HNE-induced activation of c-Jun NH2-terminal kinases" (claims 1-6 of the '064 patent) and "of down regulating the 4-hydroxynonenal (4HNE)-mediated oxidative damage associated with lipid peroxidation in a cell, the method comprising contacting the cell with an effective amount of a modulator . . . wherein 4HNE-mediated oxidative damage associated with lipid peroxidation in the cell is down regulated" (claim 7 of the '064 patent).

Applicants submit that the method steps and outcomes of pending claims 1-6, 8, and 12-15 differ from the method steps and outcomes of claims 1-7 of the '064 patent. Thus, the methods cannot be obvious one over the other. Reconsideration and withdrawal of the rejection of pending claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 7,119,064 is respectfully requested.

Double Patenting Rejection over claims 1-810 of U.S. Patent No. 6,500,798

Claims 1-6, 8, and 12-15 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No.

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6,500,798 (the '798 patent). This rejection is respectfully traversed.

Applicants submit that claims 1-6, 8, and 12-15 of the instant application and claims 1-8 of the '798 patent are drawn to methods that are patentably distinct from each other because the methods steps and outcomes of claims 1-6, 8, and 12-15 of the instant application when compared to claims 1-8 of the '798 patent are wholly different.

Specifically, as previously discussed, the pending claims of the instant application are drawn to methods "for inhibiting apoptosis in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor . . . wherein the apoptosis inhibitor inhibits apoptosis in the cell" (claim 1-6 and 8) and "for protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of a compound . . . wherein the compound protects the cell against DNA damage" (claims 12-15).

In contrast, claims 1-8 of the '798 patent are drawn to methods "for modulating the oxidative stress level in a cell, the method comprising contacting the cell with an oxidative stress regulator under conditions effective to decrease the level of an oxidizing species present in the cell in response to an oxidative stress compared to the same conditions when the oxidative stress regulator is not present" (claims 1-7) and "for modulating the oxidative stress level in a cell, the method comprising contacting the cell with an oxidative stress regulator under conditions effective to prevent or reduce an increase in the level of an oxidizing species in the cell in response to an oxidative stress compared to the same conditions when the oxidative stress regulator is not present" (claim 8).

As previously presented (see page 7, Amendment and Response filed August 17, 2006, and pages 6-7, Amendment and Response under 37 CFR 1.116, filed December 22, 2006), and as acknowledged by the Examiner (page 4, Office Action mailed October 25, 2006), the instant specification discloses that the induction of oxidative stress and the induction of apoptosis are mechanistically separate pathways within the cell. Thus, Applicants submit that, claims 1-8 of the '798 patent, drawn to methods of administering colostrinin, a constituent peptide of colostrinin and combinations thereof "for modulating the oxidative stress level in a cell, the

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method comprising contacting the cell with an oxidative stress regulator under conditions effective to decrease the level of an oxidizing species present in the cell in response to an oxidative stress compared to the same conditions when the oxidative stress regulator is not present" cannot make obvious the presently claimed methods, methods of administering colostrinin, a constituent peptide of colostrinin and combinations thereof for inhibiting apoptosis and for protecting against DNA damage in a cell.

In response the Examiner asserted that "[w]hile induction of oxidative stress by UVB-irradiation and the induction of apoptosis by UVB-irradiation are mechanistically separate pathways within the cells, the UVB-irradiation can cause both oxidative stress and apoptosis," thus the present method are obvious over the methods of the '798 patent (page 4, Office Action mailed October 25, 2006). Applicants respectfully submit that this reasoning makes no sense. Further, Applicants submit that this assertion does not establish the obviousness of the presently claimed methods (of inhibiting apoptosis and for protecting against DNA damage in a cell) over methods of modulating the oxidative stress level in a cell. Neither the present claims nor the claims of the '798 patent are drawn to effecting the overall effect of UVB-radiation. Rather, the present invention is drawn to effecting one mechanistically distinct effect of UVB-radiation (apoptosis), while the '798 patent is drawn to effecting another, mechanistically distinct action, (oxidative stress). Effecting one mechanism of action does not in any fashion make it obvious that a separate, different mechanism will be effected.

Applicants respectfully submit that the Examiner has failed to provide the necessary nexus to substantiate the assertion that the methods of instant claims 1-6, 8, and 12-15 (drawn to methods for inhibiting apoptosis and for protecting against DNA damage in a cell) are "obvious variations" of claims 1-8 (drawn to methods for modulating the oxidative stress level in a cell) of the '798 patent. Applicants respectfully submit that no teachings in the '798 patent, the instant application, nor in any references provided by the Examiner substantiate the assertion that methods for modulating the oxidative stress level in a cell (the '798 patent) and methods for

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inhibiting apoptosis and for protecting against DNA damage in a cell (the instant application) are obvious variants of one another.

Further, Applicants respectfully submit that the '798 patent does not support a rejection of the present claims under 35 U.S.C. §102(e) or 35 U.S.C. §103. Thus, Applicants' submit that claims 1-6, 8, and 12-15 cannot be rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of the '798 patent.

In view of the above discussion, reconsideration and withdrawal of the rejection of pending claims 1-6, 8, and 12-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,500,798 is respectfully requested.

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Summary

It is respectfully submitted that the pending claims 1-6, 8, 12-15, and 25-32 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted

By

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